

Potential Strategies to Address the Major Clinical Barriers Facing Stem Cell Regenerative Therapy for Cardiovascular Disease: A Review.

Journal: JAMA Cardiol

Publication Year: 2016

Authors: Patricia K Nguyen, Evgenios Neofytou, June-Wha Rhee, Joseph C Wu

PubMed link: 27579998

Funding Grants: Human Embryonic Stem Cell-Derived Cardiomyocytes for Patients with End Stage Heart Failure, Macaca mulatta as advanced model for predictive preclinical testing of engineered cardiac autografts and allografts

Public Summary:

Although progress continues to be made in the field of stem cell regenerative medicine for the treatment of cardiovascular disease, significant barriers to clinical implementation still exist. **OBJECTIVES:** To summarize the current barriers to the clinical implementation of stem cell therapy in patients with cardiovascular disease and to discuss potential strategies to overcome them. **EVIDENCE REVIEW:** Information for this review was obtained through a search of PubMed and the Cochrane database for English-language studies published between January 1, 2000, and July 25, 2016. Ten randomized clinical trials and 8 systematic reviews were included. **FINDINGS:** One of the major clinical barriers facing the routine implementation of stem cell therapy in patients with cardiovascular disease is the limited and inconsistent benefit observed thus far. Reasons for this finding are unclear but may be owing to poor cell retention and survival, as suggested by numerous preclinical studies and a small number of human studies incorporating imaging to determine cell fate. Additional studies in humans using imaging to determine cell fate are needed to understand how these factors contribute to the limited efficacy of stem cell therapy. Treatment strategies to address poor cell retention and survival are under investigation and include the following: coadministration of immunosuppressive and prosurvival agents, delivery of cardioprotective factors packaged in exosomes rather than the cells themselves, and use of tissue-engineering strategies to provide structural support for cells. If larger grafts are achieved using these strategies, it will be imperative to carefully monitor for the potential risks of tumorigenicity, immunogenicity, and arrhythmogenicity. **CONCLUSIONS AND RELEVANCE:** Despite important achievements to date, stem cell therapy is not yet ready for routine clinical implementation. Significant research is still needed to address the clinical barriers outlined herein before the next wave of large clinical trials is under way.

Scientific Abstract:

Importance: Although progress continues to be made in the field of stem cell regenerative medicine for the treatment of cardiovascular disease, significant barriers to clinical implementation still exist. **Objectives:** To summarize the current barriers to the clinical implementation of stem cell therapy in patients with cardiovascular disease and to discuss potential strategies to overcome them. **Evidence Review:** Information for this review was obtained through a search of PubMed and the Cochrane database for English-language studies published between January 1, 2000, and July 25, 2016. Ten randomized clinical trials and 8 systematic reviews were included. **Findings:** One of the major clinical barriers facing the routine implementation of stem cell therapy in patients with cardiovascular disease is the limited and inconsistent benefit observed thus far. Reasons for this finding are unclear but may be owing to poor cell retention and survival, as suggested by numerous preclinical studies and a small number of human studies incorporating imaging to determine cell fate. Additional studies in humans using imaging to determine cell fate are needed to understand how these factors contribute to the limited efficacy of stem cell therapy. Treatment strategies to address poor cell retention and survival are under investigation and include the following: coadministration of immunosuppressive and prosurvival agents, delivery of cardioprotective factors packaged in exosomes rather than the cells themselves, and use of tissue-engineering strategies to provide structural support for cells. If larger grafts are achieved using these strategies, it will be imperative to carefully monitor for the potential risks of tumorigenicity, immunogenicity, and arrhythmogenicity. **Conclusions and Relevance:** Despite important achievements to date, stem cell therapy is not yet ready for routine clinical implementation. Significant research is still needed to address the clinical barriers outlined herein before the next wave of large clinical trials is under way.

Source URL: <http://www.cirm.ca.gov/about-cirm/publications/potential-strategies-address-major-clinical-barriers-facing-stem-cell>